

Serial No. 08/734,443  
Filed: 17 October 1996

REMARKS/ARGUMENTS

Claims 18-19, 21-29, and 31-35 are pending. Claims 20 and 30 have been cancelled without prejudice to avoid redundancy and duplicity in the claims. Claim 18 has been amended. Support for amended claim 18 is found in originally filed claims 3 and 8, Example 2 on page 53, lines 16-30 and page 54, lines 1-2 of the specification, and in Fig. 2. A "Listing of Claims" is provided on pages 3-4.

**Claim Rejections- 35 U.S.C. § 112, First Paragraph**

Claim 18 (and claims 19-26 and 29-35 which depend therefrom) stand rejected under 35 U.S.C. § 112, first paragraph as not being enabled by the specification. In particular, the Office Action states the number of structural embodiments that are encompassed by the claims is undeterminable and the structural limitations in the claims do not confer the recited functional limitations.

Applicant respectfully traverses.

Applicant has amended claim 18 to recite a variant vascular endothelial cell growth factor (VEGF) polypeptide which is capable of binding to a VEGF receptor without significantly inducing a VEGF response, said variant polypeptide comprising an amino acid modification of at least one cysteine residue at positions 51 and/or 60 of the native VEGF amino acid sequence, wherein said amino acid modification inhibits disulfide bond formation.

It is well recognized in the law that a substantial amount of experimentation is permissible if the experimentation is routine or if the specification provides a "reasonable amount of guidance with respect to the direction in which experimentation should proceed." *In re Wands* 858 F.2d 731 (Fed. Cir. 1988)(*emphasis added*) See also *In re Angstadt* 190 USPQ 214, 218 (CCPA 1976). In particular, the disclosure of a test with every species covered by a

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claim is not necessary for establishing enablement under 35 USC § 112, first paragraph (*see In re Wands* 858 F.2d 731 (Fed. Cir. 1988).

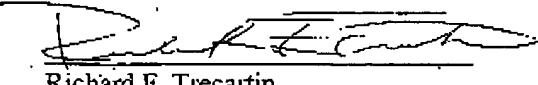
The amended claims call for one or more amino acid modifications at cysteine residue corresponding to positions 51 and/or 60 in native VEGF. The skilled artisan is aware that one or both of the identified cysteine residues can be replaced by one or more of a variety of amino acids (e.g., other than cysteine) to produce VEGF variants in which the cysteine modifications inhibit disulfide bond formation and in which the VEGF variants produced bind VEGF receptor without significantly inducing a VEGF response. The skilled artisan can also readily test the VEGF variants for the required properties using the receptor binding and vascular endothelial growth screening assays which are described in the Examples (*see e.g.*, page 44, lines 22-31, page 45, lines 1-23). Accordingly, the assays and experiments required to produce VEGF variants with amino acid modifications at cysteine positions 51 and/or 60 in native VEGF, as required by the claims, does not rise to the level of undue experimentation. Applicant therefore requests that the Examiner withdraw the enablement rejection of claim 18 (and claims 19, 21-22, 26-29 and 31-35 which depend therefrom) under 35 U.S.C. § 112, first paragraph.

#### CONCLUSION

Applicant submits that the application is in form for allowance. If there are remaining issues which the Examiner believes may be resolved by telephone, she is invited to call the undersigned attorney at (415) 781-1989.

Respectfully submitted,

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